A COMPARATIVE STUDY OF SODIUM IODID AS AN OPAQUE MEDIUM IN PYELOGRAPHY *

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The purpose of this article is to give the results of a comparative experimental study of the properties of the substances commonly used in pyelography, together with the clinical results obtained with sodium iodid. The use of this substance in roentgenography was first suggested by myself [1] in 1918. A further study confirms certain observations and conclusions made at that time and also makes necessary certain modifications, which will be noted later.

In 1906, Voelcker and Lichtenberg [2] reported the use of collargol in pyelography, and until recent years colloidal silver preparations have been used almost exclusively for this purpose. It was natural at first to consider colloidal solutions as exceptionally adapted for pyelography. For by such means, heavy elements which are relatively opaque to the roentgen ray could be introduced into the kidney pelvis in a comparatively innocuous state. An increasing experience, however, has shown that colloidal silver solutions when used in pyelography may cause necrosis of kidney tissue and produce other harmful effects. This has been commented on by a number of men, and, in fact, the men who first recommended the solution reported that in one patient operated on twenty-four hours after pyelography, some of the silver preparation was seen about the kidney pelvis and ureter. More recently, Braasch and Mann,[3] and Burns and Hopkins [4] have reported further investigations, emphasizing the danger in the use of colloidal silver preparations.

Possibly in this connection the well-known effect of electrolytes on colloidal solutions has not been sufficiently emphasized. It should be understood that many colloidal solutions of silver, at least, are very unstable in the presence of urine which always contains electrolytes in

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1. Cameron, D. F.: Aqueous Solutions of Potassium and Sodium Iodids as Opaque Mediums in Roentgenography, J. A. M. A. **70**:754 (March 16) 1918. Cameron, D. F., and Grandy, C. C.: Sodium and Potassium Iodids in Roentgenography, ibid. **70**:1516 (May 25) 1918.

2. Voelcker and Lichtenberg: Pyelographie (Roentgenographie des Nierenbeckens nach Kollargolfüllung), München. med. Wchnschr. **53**:105, 1906.

3. Braasch, W. F., and Mann, F. C.: Effects of Retention in the Kidney of Media Employed in Pyelography, Am. J. M. Sc. **152**:336 (Sept.) 1916.

4. Burns and Hopkins: A Comparative Study of the Effects of Thorium and Other Substances on the Renal Parenchyma When Retained, J. Urology **2**:145, 1918.

appreciable concentrations. When urine is added to a colloidal silver solution in a test tube, no immediate reaction is visible; but in the course of a few minutes the solution, which at first was clear, if kept at body temperature, becomes granular in appearance, and gradually a heavy precipitate forms. This fact undoubtedly accounts for the frequent finding of, and probably constant deposit of, precipitated silver throughout the kidney parenchyma after pyelography with a colloidal silver medium.

In 1913, Kelly and Lewis [5] recommended a silver iodid emulsion as a suitable medium, and this has proved quite serviceable, though it is apparent that some suitable nonviscid solution would be preferable.

In 1915, Burns [6] introduced the neutral citrate solution of thorium nitrate for this purpose. This solution, which Sollmann and Brown [7] had found to be rather inert pharmacologically, proved to have such great advantages over the other pyelographic mediums in use that it supplanted practically all of them and today is probably used more frequently than any other. The fact that this solution has been used so many times with no apparent harmful effect, and that quite good roentgenograms have been obtained is sufficient evidence as to its usefulness. This medium differs in principle from others in that it is a solution of a crystalloid and not an emulsion or colloid. However, by virtue of this fact, it loses one of the advantages of the colloids, namely, a low osmotic pressure; for it is evident that an ideal medium should have an osmotic pressure within the limits of that of a concentrated urine as a maximum and that of blood as a minimum, and, although the opacity of the thorium solution is generally sufficient, at times a more opaque medium would be preferable. Another disadvantage, though not serious, is the fact that thorium nitrate is not always easily obtained, and the standard solution is prepared with some difficulty. Again, though the viscosity of the neutral thorium citrate solution is comparatively low, still it is considerably higher than that of simple aqueous solutions of ordinary inorganic salts. This is a definite disadvantage, for it delays somewhat the filling of the kidney pelvis and so allows a greater dilution with urine and as a result the definition of the roentgenograms is impaired. However, it must be stated that in general the thorium solution is a very satisfactory pyelographic medium, and its use is attended by practically no harmful effects.

5. Kelly and Lewis: Silver Iodid Emulsion—A New Medium for Skiagraphy of the Urinary Tract, Surg., Gynec. & Obstet. **16**:707, 1913.

6. Burns, J. E.: Thorium, A New Agent in Pyelography, J. A. M. A. **64**:2126 (June 26) 1915.

7. Sollmann and Brown: Pharmacologic Investigations of Thorium, Am. J. Physiol. **18**:426, 1907.

In March and May, of 1918, I [1] suggested that certain solutions of the alkali iodids possessed certain advantages over other pyelographic mediums. In particular, it was noted that these substances were non-toxic when absorbed in ordinary amounts, and that their simple aqueous solutions were neutral in reaction, and did not form precipitates with urine. Their opacity to roentgen rays was good, their viscosity low, and they were less expensive than the other solutions in use. These solutions were not hit on by accident, but were selected after a systematic survey of the different compounds of the heavier common elements. Those which were known to be toxic or which formed precipitates with albumin or urine were excluded. Other things being equal, the substance that contained the heaviest elements and that would fulfil these conditions would be most suitable for the reason that its opacity to roentgen rays would be greater than that of solutions of other substances in the same concentration. Solutions of various compounds of bismuth, lead and strontium were tested. It was also attempted to take advantage of the property of citrates and similar organic bases to keep in solution and even render less toxic certain otherwise insoluble and toxic substances. But the results were not promising. Nor did there seem to be any suitable compound of a heavy element and one of the heavier halids, although at first it was thought that one was found in strontium iodid; but this proved to form a slowly appearing precipitate in urine. Nor were the different halid compounds other than those of iodin overlooked accidentally. It was evident that iodin, being by far the heaviest of these, would have the greatest opacity, and so could be used in weaker solutions which would have a comparatively low osmotic pressure. When the alkali iodid solutions were proposed, a 25 per cent. aqueous solution of either the sodium or potassium salt was suggested as best suited for pyelography. In the first article, it was stated that the potassium and sodium salts were used interchangeably. In the second, it was again stated that either could be used, but that the sodium salt was to be recommended. In a note [8] published in June, 1919, certain modifications of these recommendations were given. In particular, it was noted that weaker solutions could be used and that the sodium iodid was much more satisfactory.

In October, 1918, Weld [9] published an article on the use of sodium bromid in pyelography. In this article, reference was made to neither of my articles on the use of sodium and potassium iodids which appeared in earlier issues of the same journal. And although it was

8. Cameron, D. F.: The Use of Iodids in Pyelography, J. A. M. A. **72**:1737 (June 14) 1919.

9. Weld, E. H.: The Use of Sodium Bromid in Roentgenography, J. A. M. A. **71**:1111 (Oct. 5) 1918.

definitely stated in the second article that I recommended the use of the sodium salt, in the body of his article, Weld mentioned only the fact that I had recently suggested the use of potassium iodid, and added that its use in a number of cases was attended by serious reactions. Weld recommended a 25 per cent. solution of sodium bromid as being less toxic and much less expensive than potassium iodid and of about the same opacity in the same concentration. This statement concerning the relative opacity of these solutions will be shown later to need considerable modification. However, as experimental evidence in support of it, there was given a series of comparative roentgenograms of a number of alkali halids in different dilutions, together with one of a standard thorium solution.

In December, 1918, Burns and Swartz [10] showed that the ordinary dyes used in renal function tests, together with certain other substances, were absorbed quite rapidly from the pelvis of a kidney with an occluded ureter. They determined quantitatively the rate of excretion of these substances by the normal kidney under varying conditions of pressure and hydronephrosis.

In May, 1919, Weld [11] reported similar observations when pyelographic mediums were substituted for the dyes. In view of the rapid absorption of substances retained in the kidney pelvis, he emphasized the fact that the pyelographic mediums should be nontoxic. Little difference was found in the effect on renal parenchyma of solutions of sodium bromid and of potassium iodid in the same percentage concentrations. In accordance with the observations of Stockman and Charteris,[12] and many others, Weld found that potassium iodid in concentrated solution given intravenously was very toxic, while a concentrated solution of sodium bromid was quite nontoxic. Since the thorium solution also given intravenously in moderate amounts may at times be toxic, Weld concluded that the 25 per cent. sodium bromid solution was the safest and best medium so far recommended for pyelography.

It is possible that this conclusion is correct; but it is quite evident that the work so far reported in support of it is open to serious criticism. In the first place, this conclusion is based partly on the assumption made by Weld in his first article that bromids and iodids in the same concentrations have approximately the same opacity to the roentgen rays. This assumption will be shown later to be entirely erroneous in its application to pyelography. Again, it will be noted that in his comparative tests of toxicity, sodium iodid solutions received

10. Burns and Swartz: Absorption from the Renal Pelvis in Hydronephrosis Due to Permanent and Complete Occlusion of the Ureter, J. Urology **2**:445, 1918.

11. Weld, E. H.: Thesis, University of Minnesota, May, 1919.

12. Stockman and Charteris: Jour. Physiol. **26**:277.

no consideration. This is a serious omission for two reasons: first, because sodium iodid when used in pyelography or given intravenously is quite nontoxic in contrast to potassium salts whether bromid or iodid, and the toxicity of different pyelographic mediums given intravenously was one of the factors especially emphasized by Weld; second, we [13] stated that we recommended the sodium iodid in preference to the potassium salt, and gave it precedence in the title.

Since I first suggested the use of alkali iodids in pyelography, opportunity has been afforded to investigate more thoroughly the toxicity of different solutions and certain of their physicochemical properties which have an important bearing on their usefulness in pyelography. The results of this investigation, together with a report of my personal experience in the use of sodium iodid solutions in pyelography at the University Hospital, Minneapolis, will be given herewith.

EXPERIMENTAL

OPACITY TO ROENTGEN RAYS

A sufficient opacity to roentgen rays and harmlessness to the patient are the two evidently necessary characteristics of pyelographic mediums. In order to make comparable tests of the suitability of the different mediums, it is first necessary to determine what strength solutions have the same opacity under the conditions in which pyelograms are made. If the statement made by several investigators that the opacity of elements to roentgen rays varies directly with their atomic weights were true, the relative opacity problem would be very simple. On the basis of such a relation, it is evident that, with minor corrections, solutions of different substances would be equally opaque if prepared in such a way that the product of the concentration of the dissolved substance by its molecular weight were constant. And it would also follow, with minor corrections for volume, that the opacity of a 25 per cent. solution of sodium bromid, for example, would be the same as the opacity of a 25 per cent. solution of any other substance. For it is evident that in such solutions the concentration of the molecules of the dissolved substance is inversely proportional to its molecular weight, and that the product of these two quantities would be constant, except for minor corrections. In accord with this, Weld stated that 25 per cent. solutions of bromids and iodids had approximately the same opacity, showing certain roentgenograms as evidence.

In contrast to Weld's conclusion, it will be shown later that a 13.5 per cent. solution of sodium iodid is slightly more opaque than a 25 per cent. solution of sodium bromid when exposed to roentgen rays of the

13. Footnote 1, second reference.

same quality as used in pyelography, and with the filter correction which duplicates as nearly as possible the condition under which pyelograms are made.

The probable explanation of the differences here noted is simple. In the first place, it will be seen from an inspection of Weld's own illustrations that the observations he reported are incomplete. He states that the illustrations show little or no difference in opacity between the same concentrations of bromids or iodids. It is true they do not show a great difference, but still it is evident that the iodid shadows are the more dense. But there are still several other interesting features. It will be noted that the difference in density of the 12 per cent., 25 per cent. and 37 per cent. iodid solutions of each substance is comparatively slight. This means that the solutions were not exposed to roentgen rays of sufficient penetration to differentiate these solutions. But in the bromid shadows there is a much better differentiation, especially between the 12 per cent. and 25 per cent. solutions — which means that these solutions are relatively not so opaque. And, indeed, some of the 12 per cent. iodid shadows illustrated appear only slightly less dense than the 25 per cent. bromid ones. However, this difference may be brought out much more clearly. For accuracy, several precautions are necessary. The containers for the solutions should not be ordinary unstandardized bottles, the glass of which casts appreciable shadows, but should be thin-walled containers of standardized size made of uniform material of the least possible opacity. For this purpose, from a large shipment, four very thin-walled test tubes were selected whose diameters were greater than 18.2 mm. and less than 18.7 mm. The opacity of the tubes themselves to the roentgen rays used is very slight and practically constant, so that a minimum constant error is produced. The solutions themselves were made with accuracy from chemically pure materials and distilled water. The molecular as well as percentage concentration is given. The former is by far the more convenient when different dilutions are used. The neutral thorium solution was prepared according to the directions given by Burns. Thorium nitrate free from water of crystallization was used. It should be noted that it is not exactly correct to call it a 15 per cent. thorium nitrate solution as is customary, because 15 gm. of thorium nitrate in addition to a considerable quantity of sodium citrate and some alkali dissolved in a sufficient amount of water to make 100 c.c. does not make a 15 per cent. solution. It is better designated as a $\frac{5}{16}$ molar solution of thorium nitrate. The exposure to roentgen rays was made under conditions which duplicate as far as possible those under which pyelograms are made. A great error results if rays of low penetration are used. It is well known and easily demonstrated that quite light substances such as hair and gauze, not to mention the lighter elements like sodium, magnesium and aluminum, for example, will cast quite dense shadows if rays of very low penetration are used, while their shadow is entirely invisible or scarcely visible when the rays used are sufficiently "hard" to penetrate in quantity the human body at the level of the kidney. From this it is evident that in comparative experimental tests of opacity not only must the penetration be as great as that used in pyelography, but also all of the soft rays must be filtered off by suitable means, since they are filtered off in passing through the body. Figure 1 illustrates the relative opacity of the different solutions under the conditions indicated, and is only one illustration chosen from a number made under similar conditions and with the same results. These solutions were also exposed to "softer" rays,

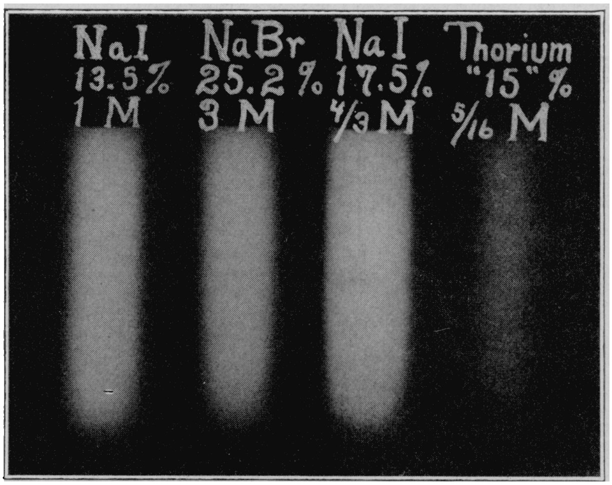

Fig. 1.—The relative opacity of the solutions indicated under the conditions noted (Coolidge tube, 20 inches distance, 4.5 inches alternate spark gap, 38 milliamperes current, 5 seconds exposure). A 4 mm. aluminum filter was placed in front of, and a similar thickness behind, the tubes, corresponding, in general, to the obstruction due to the abdominal walls encountered in practice. The time of exposure, penetration and current are the same as those used generally in pyelography. The thorium shadow on the original negative was relatively denser, and the contrast between the various shadows was less distinct, than in this illustration. Other roentgenograms made under the same conditions except with a 6 inch spark gap and 20 milliampere current showed the same result except that the iodid shadows were relatively still more intense. The roentgenograms made with 3 inches penetration and less showed denser thorium and bromid shadows.

that is, to rays from a tube with an alternate spark gap of only 3 inches. This has the effect of making the bromid and thorium shadows relatively denser, especially when none of the very soft rays are filtered off by aluminum plates.

From several series of experiments, of which only one plate is reproduced, it may be stated definitely that with conditions for pyelography duplicated, the molar (13.5 per cent.) solution of sodium iodid has the same or even a trifle greater opacity than a 3 molar (25.2 per cent.) solution of sodium bromid, and further, that these two solutions have a definitely greater opacity than the standard neutral thorium citrate solution.

Aside from its bearing on pyelography, this result in the case of iodids and bromids is of interest in that it agrees closely with the results obtained by various physicists who have investigated the opacity of elements to roentgen rays by different and more exact methods. The most convenient summary of results of experiments in this line will be found in two comparatively recent publications by Auren.[14] Certain of his results, with which my own are in accord, are of particular interest. He states that iodin with two or three other elements, not including bromin, possesses the property of selective absorption of roentgen rays especially marked with the rays of high penetration. In other words, iodin and the compounds of iodin are much more opaque to the roentgen rays than would be expected from the known properties of this element and its position in the periodic table. Auren gives the "roentgen-ray atomic absorption coefficient" of practically all of the ordinary elements, and from this table the opacity of any concentration of the commoner substances can be calculated. A few of these values of particular interest in this connection are transcribed in Table 1. The molecular absorption coefficient of water is arbitrarily taken as unity.

The values given in Table 1 represent the average opacity of the elements to comparatively soft rays. Of particular interest are the values for different wave lengths. These values, which show the selective absorption property of iodin, are given in Table 2.

The "hardness" of the rays (which varies inversely with their wave lengths) is represented by the thickness of the aluminum filter indicated above the absorption coefficient values. The penetration used in pyelography corresponds to that represented in the third and fourth columns. The values shown in Table 2 are seen to agree almost exactly with those obtained by myself as shown in Figure 1. That is, one iodin atom has the opacity of three bromin atoms to waves of this length. It should be added that the plates that I exposed to softer rays showed a relatively greater opacity of the bromid and thorium solutions, which agree closely with the values shown in column 1. When soft rays are used, the shadows of the thorium and bromid solutions are more dense than the molar iodid solution. But it is very

14. Auren, T. E.: Notes on the Absorption of X-Rays, Phil. Mag., Series 6, **33**:471; The Absorption of X-Rays, ibid. **37**:165.

important to note that such rays are much softer than those used in pyelography, and the absorption values so obtained are in no way applicable in pyelography.

Auren and most physicists in their work measure the intensity of transmitted roentgen rays by the degree of ionization produced in a protected chamber behind the absorbing medium. This method of measuring intensity is more accurate than the photographic method, but in testing pyelographic mediums the photographic method is of relatively greater value. However, from the work of Barkla and

TABLE 1.—Roentgen-Ray Atomic Absorption Coefficient of Various Elements

Element	Atomic Weight	Atomic Number	Absorption Coefficient
Hydrogen	1	1	0.05
Oxygen	16	8	0.9
Sodium	23	11	1.9
Aluminum	27	13	3.4
Potassium	39	19	11.1
Calcium	40	20	14.4
Bromin	80	35	154.0
Silver	108	47	300.0
Iodin	127	53	315.0
Lead	207	82	569.0
Thorium	232	..	(1,000, approximately, by interpolation, D. F. C.)
Uranium	239	92	1,123

TABLE 2.—Values of Different Wave Lengths

Element	Atomic Weight	Atomic Number	Absorption Coefficient			
			I 1.2 mm. Aluminum Filter	II 2.5 mm. Aluminum Filter	III 5 mm. Aluminum Filter	IV 10 mm. Aluminum Filter
Bromin	80	35	152.5	137.7	119.9	100.0
Iodin	126	53	226.0	352.0	356.0	366.0

Martyn[15] and others, it is known that the photographic effect of rays is rather variable. Soft rays produce relatively too great, and hard rays relatively too little effect on the photographic plate. Irregularities in the photographic film, secondary radiation induced and exposure to heterogeneous rays are also disturbing factors. Under similar conditions, however, the results obtained by the two methods are not widely divergent. And an examination of the results makes evident the fact that no simple relation exists between either the atomic weight or the atomic number of an element and its absorption coefficient. Bragg and Pierce,[16] in an investigation of this relationship, came to the con-

15. Barkla and Martyn: Photographic Effect of X-Rays, Phil. Mag., Series 6, **25**:296.

16. Bragg and Pierce: Absorption Coefficients of X-Rays, Phil. Mag., Series 6, **28**:626

clusion that the atomic absorption coefficient of an element varied with the fourth power of the atomic number, but, as yet, there is no generally accepted formula connecting these values. It is important that these facts should be emphasized in medical literature for, through ignorance of them, a number of incorrect statements have been made in recent medical publications involving the question of the relative opacity of pyelographic mediums. It will be seen that among the lighter elements the roentgen-ray opacity increases relatively slowly with atomic weight, while with the heavy elements this increase is much more marked.

In general, for ordinary pyelographic work, the molar (13.5 per cent. solution of sodium iodid and the 3 molar [25.2 per cent.]) solution of sodium bromid have the same opacity and the opacity of the standard thorium solution is definitely less, corresponding approximately to that of a 10 per cent. sodium iodid solution. And from the data given, the important fact is obvious that with increasing roentgen-ray penetration the relative opacity of the iodid solution increases and the opacity of the bromid and thorium solutions decreases. Moreover, this difference is not slight but is very marked, and constitutes one of the real advantages of the iodid solution in pyelography.

TOXICITY

In contrast to the comparative ease and accuracy with which the opacity of these solutions can be determined, the determination of their relative toxicity is less satisfactory, especially since the toxic effects of none of them are marked. But it is evident that in order to obtain comparable results, solutions of the same opacity must be used. It is also evident that the toxicity of these solutions may be due either to the specific action of the substances in solution on different living tissues, or to the effect of the hypertonic solution in which the substances are carried, or to a combination of these two effects.

The effect of these solutions on the kidney itself is naturally the first to be determined. For this test, normal and hydronephrotic dog kidneys were used, and both functional and anatomic changes were determined when possible.

RESULTS OF EXPERIMENTS

EXPERIMENT 1.—A cannula was inserted into each ureter of a dog which was kept under ether anesthesia. One c.c. of phenolsulphonephthalein was given intravenously. Diuresis was stimulated by giving Ringer's solution and hypertonic glucose solution [17] intravenously. In twenty-five minutes, the urine excreted

17. Woodyatt, R. T.; Sansum, W. D., and Wilder, R. M.: Prolonged and Accurately Timed Intravenous Injections of Sugar, J. A. M. A. **65**:2067 (Dec. 11) 1915.

by the right kidney contained 32 per cent. of the dye, the left 35 per cent. Thereupon the right kidney pelvis was filled with a molar solution of sodium iodid which was kept under a pressure head of from 34 to 32 inches of the solution for twenty minutes. The secretory pressure of the kidney was approximately 32 inches, since the height of the fluid fell gradually from 34 inches to that level, where it remained quite constant. The blood pressure was recorded continuously throughout the experiment and was not affected materially at any time as a result of the intravenous injections or distention of the kidney pelvis. The urine collected during this time at five minute intervals from the left kidney showed no iodid when tested with chloroform, acetic acid and hydrogen peroxid.

After the expiration of twenty minutes, the pressure of the sodium iodid solution on the right kidney pelvis was discontinued and a rest of five minutes

Fig. 2.—Right pyelogram with molar (13.5 per cent.) solution of sodium iodid; capacity of pelvis, 10 c.c. Patient was an unusually heavy man.

allowed. One c.c. of standard phenolsulphonephthalein solution was again given intravenously, and the urines were collected for fifteen minutes. In this period, the right kidney excreted 26 per cent., and the left, 28 per cent.

The right kidney pelvis was then kept distended for fifteen minutes with a 3 molar (25.2 per cent.) solution of sodium bromid under a head of from 36 to 34 inches, the secretory pressure of the kidney apparently having risen somewhat for the specific gravity of the bromid solution is appreciably higher than that of the iodid. At the end of this period a functional test was again made, the right kidney excreting 27 per cent., and the left, 31 per cent., of the dye in fifteen minutes.

Experiment 2.—Experiment 1 was in part repeated on a second dog, but unfortunately the specimens of the preliminary functional test were lost. After the right kidney pelvis had been kept distended for twenty-five minutes with a molar sodium iodid solution at secretory pressure, the functional test was repeated, the right kidney excreting 40 per cent., and the left 40 per cent. of phenolsulphonephthalein.

At the conclusion of these experiments, the kidneys were removed and examined for gross and microscopic changes, but none were noted. In these experiments no immediate diminution in renal function, as indicated by the phenolsulphonephthalein test, was observed after the kidney pelvis was kept distended for from twenty to twenty-five minutes with molar sodium iodid, or fifteen minutes with 3 molar sodium bromid solution at the secretory pressure of the kidney. It will be noted that both the time of the distention and the pressure are several times as great as occurs in practice when pyelograms are made, i. e., if the medium is injected by the gravity method.

Experiment 3.—To duplicate, after a fashion, the situation resulting when the pyelographic medium is introduced into a kidney pelvis which fails to empty itself immediately, the right kidney pelvis in each of seven dogs was filled with 4/3 molar (17.5 per cent.) sodium iodid solution under 12 inches pressure. The amount of solution introduced averaged about 2 c.c. The ureter was then doubly ligated and divided. The right ureter in an eighth dog was doubly ligated and divided to serve as a control. All of the dogs survived until killed, and with no apparent harmful effects as far as general health was concerned. The first specimen of voided urine from the injected dogs showed a strongly positive test for iodin in each case. The test remained positive for at least twenty-four hours, no test being made at later times. After the injections, the animals were killed at periods varying from forty-five minutes to seventy-five days. The kidneys were removed and the contents of the right pelvis tested for the presence of iodids. The test for iodids in the pelvic contents of the ligated kidney was negative in the five dogs that were allowed to live two hours or over after injections. Iodid was present in the two specimens obtained from dogs killed in forty-five minutes and one and one-half hours, respectively. The rate of absorption was not thoroughly investigated, but in instances in which there was good diuresis and when the iodid solution had been introduced into the right kidney pelvis with a syringe and probably under higher pressure than usual, iodid appeared in the urine excreted by the left kidney five minutes later. At other times, however, when the right kidney pelvis was kept distended with the iodid solution under an even pressure up to the secretory pressure, no iodid was found in the urine from the left kidney excreted in from fifteen to twenty minutes after the injection.

The absorption from a hydronephrotic kidney was also tested. The animal, whose right ureter had been occluded for seventy-five days, was found to have a large palpable tumor appearing in the right upper part of the abdomen. This was found to be a hydronephrotic kidney sac containing 450 c.c. of fluid under 9 inches of pressure — about one third or one fourth of the normal secretory pressure found. The fluid was evacuated through the ureter. Following intravenous injection of saline and hypertonic glucose solution, the left kidney showed a good diuresis, but no fluid was excreted by the right. At this time 50 c.c. of 4/3 molar (17.5 per cent.) sodium iodid solution was introduced into the hydronephrotic sac which was, thereby, only slightly distended. Urine collected from the left kidney in ten, fifteen and twenty minutes showed iodid in rapidly increasing amounts, and in much greater concentration than found previously when the iodid solution was introduced into normal kidney pelves.

COMMENT

I do not now intend to advocate the use of potassium iodid solution for pyelography; but in view of the rapidity of absorption of substances from the kidney pelvis and the well-known toxicity of potassium

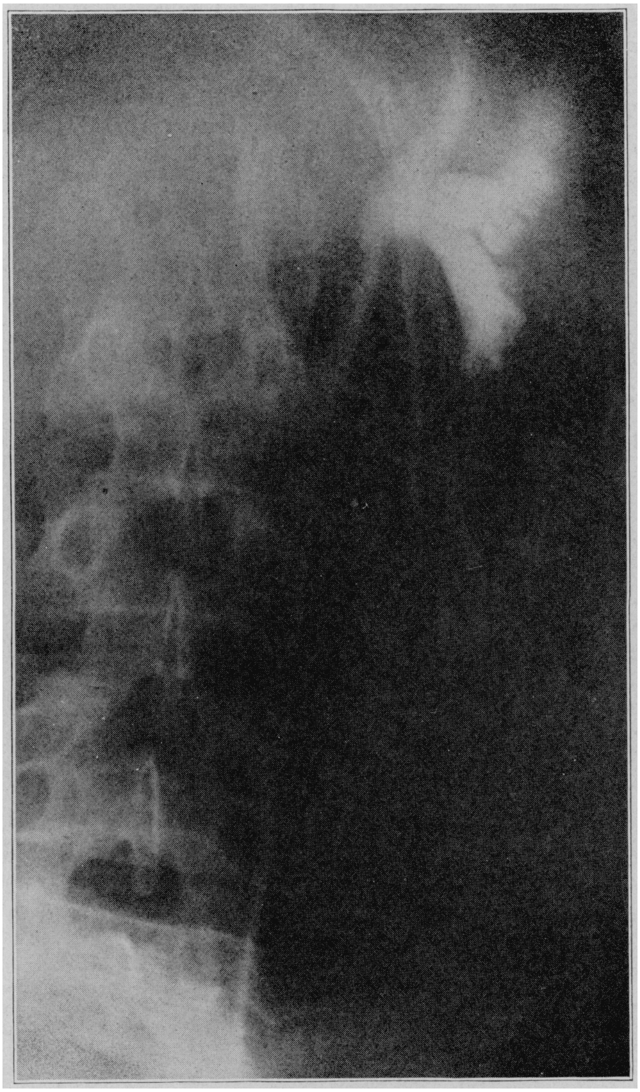

Fig. 3 (Miss H.).—Left pyelogram with four-thirds (17.5 per cent.) solution of sodium iodid. Distinctness of minor calices may be noted, and their shape compared with that in Figure 4.

salts when given intravenously, the effect of the introduction of strong potassium iodid solution into the hydronephrotic sac was tested.

Thirty c.c. of a 25 per cent. solution of potassium iodid was introduced into the hydronephrotic sac which had been evacuated of all contents. A blood pressure tracing taken for the following ten minutes showed no circulatory changes. Likewise, no toxic effects of any kind were noted when a normal kidney pelvis was kept distended with a 25 per cent. solution of potassium iodid under 34 inches of pressure for a period of twenty minutes. As a matter of fact, in order that toxic

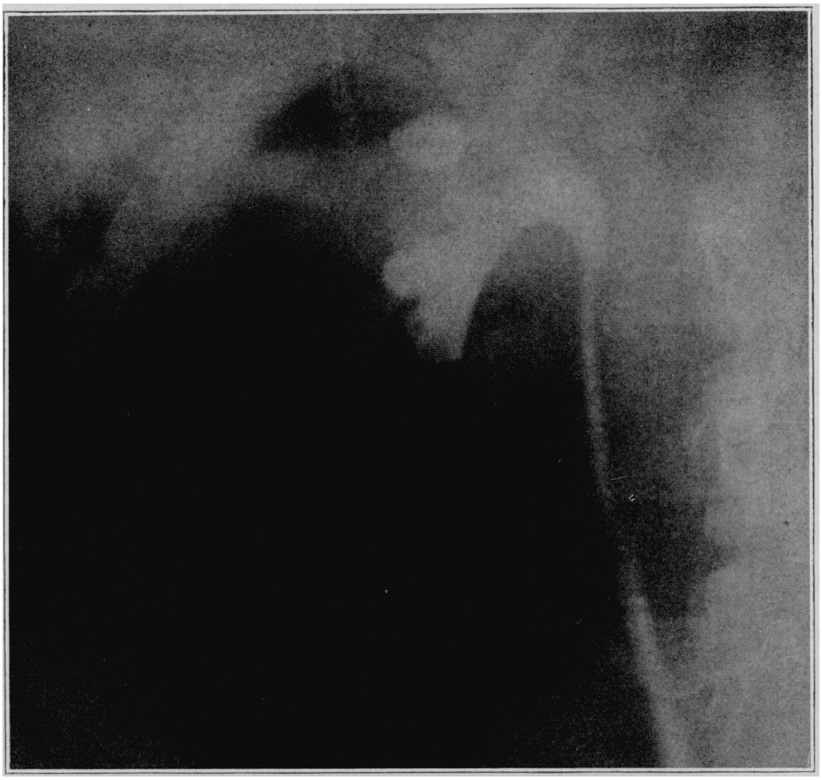

Fig. 4 (Miss H).—Right pyelogram with 17.5 per cent. sodium iodid solution. History of repeated right-sided kidney colic.

effects should be produced, the absorption of potassium iodid from the kidney pelvis would have to be more rapid than from the gastro-intestinal tract.

Pathologically, the kidneys whose pelves had been injected and whose ureters had been ligated showed very marked changes which varied in degree with the time elapsing after the ureteral occlusion, and showed all stages of hydronephrosis. But any changes which might have been due to the presence of sodium iodid were completely overshadowed by the effects of occluding the ureter, since the changes following occlusion of the ureter alone could not be distinguished from those in which sodium iodid solution had also been injected.

This series of experiments shows that animals may live in apparently good health after the function of one of two normal kidneys has been lost by occlusion of its ureter, and that a 4/3 molar (17.5 per

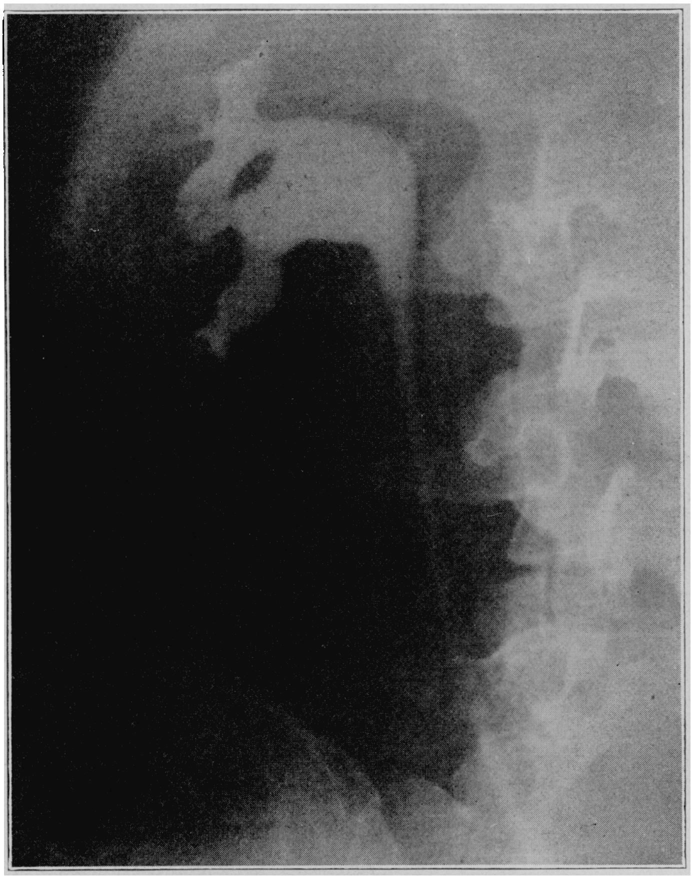

Fig. 5 (Miss C).—Right pyelogram with 17.5 per cent. sodium iodid solution; thin patient.

cent.) solution of sodium iodid introduced into the pelvis of the kidney whose ureter has been occluded is absorbed, as a rule, in about two hours and causes no apparent harm, similar results being noted by Burns and Weld when other solutions were used. Rough quantitative tests also showed in the one case investigated that the total amount of sodium iodid absorbed in a given time from a large hydronephrotic sac filled with the iodid solution was much greater than the amount absorbed in the same time from the pelvis of a normal kidney whose ureter had been occluded and which had been filled with iodid solution of the same strength. The absorption of potassium iodid from the hydronephrotic sac containing 30 c.c. of a 25 per cent. solution was not sufficiently rapid to cause apparent circulatory changes, nor were there any effects noted when a normal kidney pelvis was kept distended with a 25 per cent. potassium iodid solution under 34 inches of pressure.

TOXICITY OF MEDIUMS GIVEN INTRAVENOUSLY

The true tests of toxicity of pyelographic mediums should be made by determining the effects of these solutions when introduced into normal and diseased kidneys or ureters. However, it adds somewhat to the factor of safety if these solutions are not toxic when introduced directly into the blood stream in such amounts and concentrations as might occur from absorption from the kidney pelvis or might result from the accidental use of too great pressure in injection of the solution into the pelvis.

In the first experiment, a dog weighing 34 pounds was used. The intravenous injection of 5 c.c. of a 4/3 molar sodium iodid solution in thirty seconds caused no changes in the blood pressure curve. The subsequent injection under the same condition of the same amount of 3 molar sodium bromid and of the standard thorium solution was likewise without effect. The injection of 5 c.c. of molar potassium iodid solution caused a definite fall in blood pressure with gradual recovery. The experiment was repeated on the same dog, 16 c.c. of each solution being given in forty-five seconds. The injection of the 4/3 molar sodium iodid and of the 3 molar sodium bromid was without effect. Following the injection of the thorium solution, a very definite fall in blood pressure occurred, with gradual recovery. The dog died in fifteen seconds after the beginning of the injection of the molar potassium iodid. In other experiments, the amount of bromid and iodid solution given was considerably increased. No marked effects were caused when 50 c.c. of a 25 per cent. sodium iodid solution were injected in eight minutes in a 25-pound dog, the blood pressure curve rising slowly. The same amount of a 25 per cent. sodium bromid solution was given in ten minutes in a 30-pound dog, without apparent effect, thus confirming the result obtained by Weld. This dog died following the injection of 2 c.c. of 25 per cent. potassium bromid solution.

From this series of experiments, it is seen that 25 per cent. solutions of sodium iodid and sodium bromid, given intravenously in amounts up to 50 c.c. in 30-pound dogs produce very little immediate effect. It will be noted that this iodid solution is of nearly twice the concentration which is recommended for pyelography. The standard thorium solution is relatively nontoxic, but definitely more toxic when given intravenously than either the sodium iodid or sodium bromid solutions. Potassium salts, as has long been known, are very toxic when given

Fig. 6 (Mrs. R.).—Triple pyelogram with 17.5 per cent. sodium iodid: thin patient. Fused kidney with two pelves and ureters on the left. The condition was first diagnosed and the three ureters catheterized by Dr. F. R. Wright.

intravenously. It should be noted that in his comparative toxicity tests with sodium bromid, Weld used potassium iodid throughout instead of sodium iodid; and the marked toxicity of potassium iodid intravenously, which he commented on and on which he based his serious objection to the use in general of iodids in pyelography, is due to the potassium ion.

It may be noted in passing that intraperitoneal injection of 20 c.c. of molar sodium iodid, 3 molar sodium bromid and standard thorium solution showed no constant differences in their effects produced within the two hours following the injection.

In general, the pure sodium iodid and bromid solutions were found to be strikingly nontoxic. It is probable, however, that these and the potassium salt solution, if desired, could be made still less toxic by the addition of small amounts, in correct proportion, of other salts, e. g., of calcium or magnesium, which Jacques Loeb,[18] Mathews [19] and others have shown to have a marked antagonistic effect on the toxicity of potassium and sodium ions. On the whole, the experiments made show that there is no marked difference in specific toxicity of iodids and bromids, the cation being the same, when solutions of the same percentage concentration are used. Of course, it must be noted that a 25 per cent. iodid solution has a much lower osmotic pressure than a similar 25 per cent. bromid solution; also that a 25 per cent. iodid solution is much more concentrated than that recommended for pyelography. Very detailed experiments in the toxicity of different anions and cations in relation to their solution tension and its relation to osmotic pressure are reported by Mathews.[20] The iodid ion is considered only slightly more toxic than the bromid ion.

OSMOTIC PRESSURE

The other possible cause of toxic effects resulting from the use of these solutions is their osmotic pressure. Of the several ways in which osmotic pressure of solutions may be determined, the most feasible for the solutions concerned is the freezing point method. Very accurate results may be obtained. The osmotic pressure of a solution is directly proportional to the depression of the freezing point below that of the pure solvent. The solutions tested were those used in the experimental work already reported. The depression of the freezing point of the iodid and thorium solutions noted in Table 3 is twice the value found for the solutions diluted with an equal volume of distilled water. This involves a slight but negligible error.

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18. Loeb, Jacques: The Dynamics of Living Matter, New York, Columbia University Press, 1906.

19. Mathews, A. P.: The Toxic and Antitoxic Action of Salts, Am. J. Physiol. **12**:419, 1904-1905.

20. Mathews, A. P.: The Nature of Chemical and Electrical Stimulation, Am. J. Physiol. **11**:455, 1904; The Relation Between the Solution Tension, Atomic Volume and the Physiological Action of the Elements, ibid. **10**:290, 1904.

According to Jones and Bassett,[21] the freezing point of solutions of sodium iodid and sodium bromid of the same molecular concentration is approximately the same and the actual lowering is greater than the theoretical, owing to the formation of hydrates. For comparison, the usual values for the freezing point of blood and of a concentrated urine may be taken as — 0.56 C. and — 2.70 C., respectively. The value for a very concentrated urine is considerably higher.

It is evident from these data that the molar solution of sodium iodid has a somewhat higher osmotic pressure than a concentrated urine, but in this respect comes much nearer than any of the other solutions to fulfiling the ideal requirements. It will be noted that the bromid solution has an osmotic pressure more than three times that of the iodid. This fact is of considerable importance, for it is well known that tissues are injured by being exposed to hypertonic solutions.

TABLE 3.—Freezing Points of Iodid and Thorium Solutions *

Solution	Freezing Point, Degrees C.
Sodium iodid, molar (13.5%)	—3.78
Neutral thorium, standard, Prep A	—5.52
Neutral thorium, standard, Prep B	—5.61
Sodium bromid, 3 molar (25.2%)	—13.47

* The value for 3 molar sodium bromid given is calculated from the data given by Jones and Getman (Ueber das Vorhandensein von Hydraten in konzentrierte wässerige Lösungen von Electrolyten, Ztschr. f. physik. Chem. **49**: 385.

IRRITATION

The pain or discomfort which might be caused by the action of various solutions on sensory nerves of the kidney pelvis and ureter is somewhat difficult to determine, owing to the fact that the pain may be caused by one or more of several other factors, such as the catheterization alone or the overdistention of the kidney pelvis. It is well known that the pain during and after cystoscopy and ureteral catheterization alone may be quite severe. Again, the intrapelvic pressure need not be higher than the secretory pressure of the kidney under certain circumstances to cause colic. Therefore, pain during or following pyelography must not be attributed to the nature of the pyelographic medium unless the other causes are definitely known to be absent. Also, increasing experience shows that overdistention of the kidney pelvis, even though the gravity method is used, is a frequent cause of discomfort.

21. Jones and Bassett.: The Approximate Composition of the Hydrates Formed by Certain Electrolytes in Aqueous Solutions at Different Concentrations, Am. Chem. J. **33**:534, 1905.

The relative sensory stimulation produced by the various pyelographic mediums on tissue supplied with special sensory nerves can be easily determined. Very definite and striking results are obtained when the tongue is immersed in the various mediums. The standard

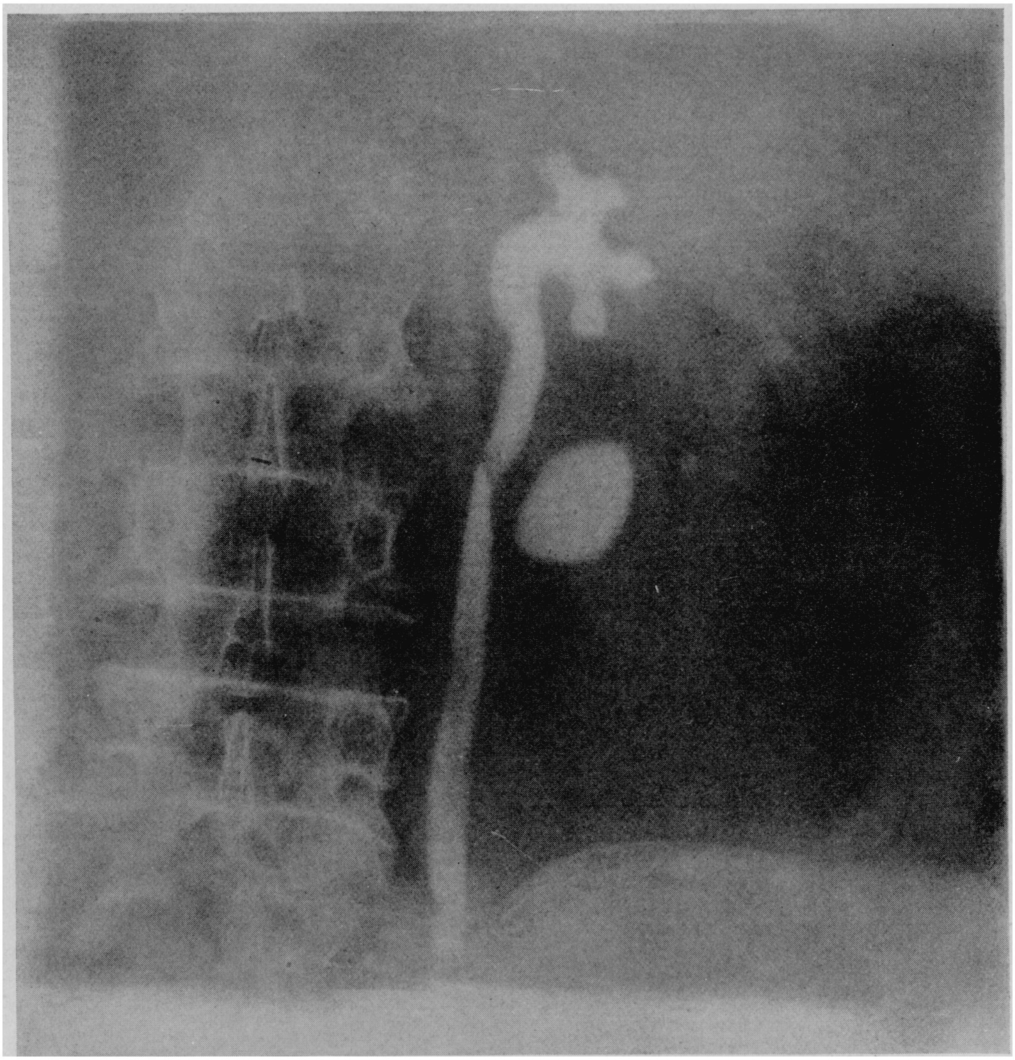

Fig. 7 (Mrs. R.).—Upper pelvis on left filled with 1% per cent. sodium iodid solution. Shadow of two stones and lower pole of the kidney distinctly seen.

neutral thorium solution which has a high sodium citrate content in addition to the thorium nitrate is surprisingly mild to the tongue and almost tasteless. A molar solution of sodium iodid has a distinctly saline taste and causes no further apparent stimulation, even when the tongue is kept immersed in it for some time. The 3 molar sodium bromid solution, which Weld advocated as being quite bland, causes a definitely more intense stimulation on the tongue, at least, than that produced by the sodium iodid solution. It was found, however, that solutions of potassium salts were always distinctly more irritating to the tongue than solutions of the same concentration of sodium salts. This fact was overlooked in testing the stronger solutions recommended in my first articles, and now constitutes one of the main objections to the use of either potassium iodid or potassium bromid solutions. The calcium and strontium salts which also were tested were more or less irritating to the tongue. It is obvious, of course, that the kidney pelvis, which is insensible to presence of urine, is not nearly so sensitive to chemical stimulation as the tongue.

VISCOSITY

The ease with which these various solutions flow through small catheters and spread and diffuse into the smaller calices of the kidney pelvis depends primarily on their viscosity.

TABLE 4.—Relative Viscosity of Various Solutions

Solution	Viscosity
Distilled water	28.0
Molar sodium iodid	29.0
3 molar sodium bromid	31.5
Neutral thorium	50.0

The viscosity of the solutions was determined by the viscometer used for blood work. The figures given in Table 4 represent the time in seconds required for the solution tested to flow from the graduated chamber through the capillary exit. These values represent the relative viscosity of the solutions noted. The whole apparatus and solution were immersed in a water bath kept at body temperature.

It is obvious from these results that distilled water and the iodid solution have approximately the same viscosity. The bromid solution shows a slight increase. The thorium solution is definitely more viscid. This is not so serious, but, nevertheless, is a definite handicap when the easy and rapid flow and diffusion of the solution under a minimum pressure is desired. From the figures given, it is seen that a given quantity of the iodid solution would flow into the kidney pelvis in much less time than would be required for the same quantity of the thorium solution, the pressure head being the same. In this connection, it must be remembered that the kidney is secreting urine continuously, and the concentration of the pyelographic medium in the pelvis is lowered in proportion to the time consumed in filling it. And thus the opacity of the standard thorium solution which was determined experimentally in the test tube is considerably diminished in practice, through relatively greater dilution with urine in the kidney pelvis.

CLINICAL RESULTS

To Dr. A. C. Strachauer I am indebted for the opportunity of putting to practical use solutions of sodium iodid in pyelography, the work being carried out on the surgical service at the University Hospital, Minneapolis.

The results given here are based entirely on my experience in using for pyelography sodium iodid in concentrations varying from 20 per cent. to 13.5 per cent. in strength. In all, twenty-two pyelograms and ureterograms were made. At the beginning of the work the stronger solutions were used, but it was soon seen that the results were very good with weaker solutions, and lately the 13.5 per cent. solution has been used altogether. The results with it have been so satisfactory, even when it was put to a severe test in unusually heavy patients, that it seems probable that no stronger solution need ever be used, and in thin patients still weaker ones would suffice. It will be noted that a molar solution of sodium iodid is formed when 15 gm. of the salt is dissolved in a sufficient amount of water to make 100 c.c., and this will be found to contain 13.5 per cent. sodium iodid by weight. Likewise, the 17.5 per cent. and 4/3 molar solutions are identical and are formed by dissolving 20 gm. of salt in a sufficient amount of water to make 100 c.c.

The pyelograms obtained were uniformly good. They were all made with the ordinary gas tube, the alternate spark gap varying from 4 to 4½ inches. For the excellent roentgenographic work displayed in making the pyelograms as well as in the investigation of the relative opacity of numerous solutions, credit is due Miss Bagamill of the University Hospital. The average quality of the pyelograms is shown in the accompanying illustrations, which do not represent in any way exceptional results, for the pyelograms illustrated, with the two exceptions noted, were obtained with patients well above the average in weight. The solution was always injected by the gravity method, the exposure being made while the kidney pelvis was being filled. The apparatus described by Thomas [22] is well suited for this purpose. In this connection it is well to emphasize the point made by several men that the technical results are very much better if the exposure is made while the kidney pelvis is still being filled. This point must not be overlooked if good results are desired. On two occasions, I attempted to make a double pyelogram, using a buret with a single catheter

22. Thomas, G. J.: An Apparatus for the Injection and Lavage of the Pelves of the Kidneys and the Ureters, J. A. M. A. **60**:184 (Jan. 18) 1913.

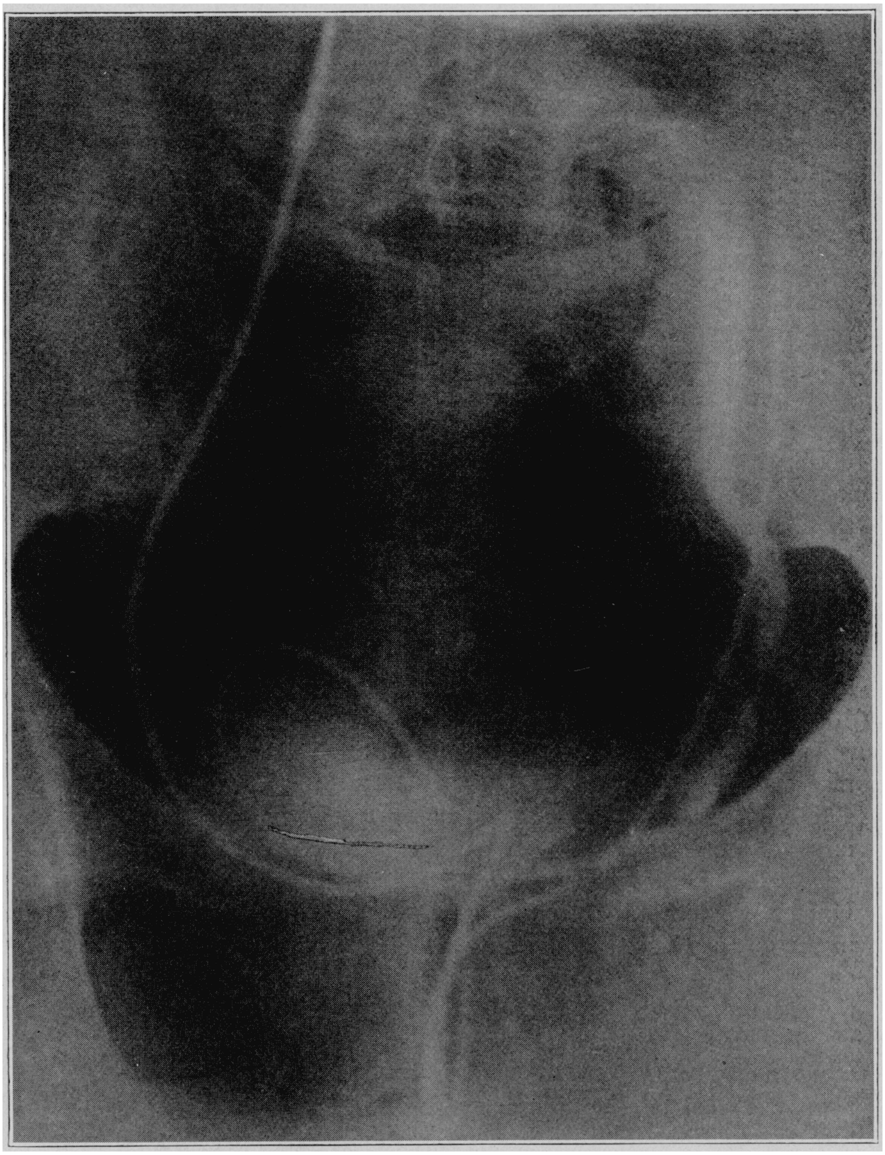

Fig. 8 (Mrs. R.). —Left lower ureterogram. Irregular shadows, shown near the bladder in the original roentgenogram, are localized by this ureterogram. The patient subsequently passed four small stones spontaneously. It will be noted that the upper pelvis of this kidney and its ureter were free from stones. A 17.5 per cent. sodium iodid solution was used.

needle. After the first pelvis was filled, the catheter was occluded by a small wooden cork and the needle transferred to the other catheter. In each instance, the technical result was poor on the side first filled. The amount of solution introduced into the kidney pelvis varied from 4 to 10 c.c., the least amount introduced (4 c.c.) of the 4/3 molar solution represented the capacity of a polycystic kidney pelvis, and an excellent pyelogram was obtained. In no case in my rather limited experience with the molar solution has a poor pyelogram resulted as the result of insufficient opacity of the medium. But if experience should show that a more opaque medium is desirable at times, it should be remembered that the 4/3 molar (17.5 per cent.) solution of sodium iodid may be used with perfect safety, and that it is much more opaque than either the 25 per cent. bromid or standard thorium solution.

To determine the amount of discomfort or pain produced, the patients were carefully observed and questioned while the pyelograms were being made and afterward. A reasonable allowance was made for the distress occurring after cystoscopy and ureteral catheterization alone. The results may be thus summarized: In no instance was there any increase whatever in discomfort noted or complained of while the first 4 or 5 c.c. of any of the iodid solutions used were being introduced into the kidney pelvis. Several patients, on whom differential functional tests had just been made, were unable to distinguish any new sensations whatever, either during or subsequent to the filling of the pelvis. Figure 2 is a pyelogram of such a patient, in whose kidney pelvis 10 c.c. of the molar solution was introduced. A few of the patients began to have increasing distress when the injection was continued after 4 or 5 c.c. of solution had been introduced. In view of the absolutely painless procedure in a number of cases, I am convinced that the distress in these instances was caused entirely by overdistention of the kidney pelvis, it being evident that only a small amount of solution might cause an overdistention of a pelvis which, at the same time, was being rapidly filled with urine. It was soon learned, as has been especially emphasized by Braasch,[23] that the injection should not be carried so far as to produce pain; thus far, the small amount of solution injected painlessly in such cases has been sufficient to outline the pelvis, though it is evident this might be unsatisfactory if one were dealing with a hydronephrosis. During the twenty-four hours after pyelography, some of the patients have complained of distress, occasionally quite severe, felt in the kidney region and along the ureters, but this trouble, except in those who had had an evident overdistention of the kidney pelvis, could be considered no more severe than that occasionally produced by ureteral catheterization alone. On the whole,

23. Braasch, W. F.: Pyelography, Philadelphia, W. B. Saunders Company.

it may be stated that no increased discomfort is caused by the introduction of a molar, or 4/3 molar, solution of sodium iodid into the human kidney pelvis, provided no overdistention is produced.

It was also considered of interest to determine what changes, if any, are produced on the function of the human kidney, the pelvis of which has been filled with the iodid solution. It will be recalled that this procedure had no effect on the kidney function in the dog. In Table 5, the total renal function before and after double pyelography is given. The total functional change after single pyelography is not given, as it would be of little significance, since an appreciable damage to one of two good kidneys might produce little or no change in total function.

From these results it is evident that the use of sodium iodid in pyelography causes no diminution of renal function demonstrable by the ordinary functional tests.

TABLE 5.—Total Renal Function Before and After Double Pyelography

Patient	Original Phenolsulphonephthalein Excretion, per Cent.	Procedure	Solution Used, per Cent.	Phenol-sulphone-phthalein Excretion Afterward, per Cent.
Mr. S.	45	2 double pyelograms	17.5 13.5	 43
Mrs. R.	..	2 triple pyelograms	17.5	64
Miss V.	75	Double pyelogram	17.5	72
Miss D.	65	Double pyelogram	17.5	71
Mrs. W.	Blood urea nitrogen, 12 mg.	Single pyelogram; other ureter occluded	17.5	11.5 mg.
	Creatinin, 1 mg.	....	....	0.85 mg.

CHOICE OF SOLUTIONS

In view of the effect of colloidal silver solutions on the renal parenchyma, as has been shown by various reports in recent medical literature, their use should be discontinued. Braasch and Mann,[3] in particular, have reported the results of comparative study of the effect of various mediums on the kidney. In addition to their toxic effects, they are expensive, viscid, possess undesirable physical properties, and are unstable in the presence of urine.

In being free from toxic and irritating effects and in giving fairly good technical results, the neutral thorium solution recommended by Burns is entirely satisfactory so far as I am aware. The fact that it had been used at one hospital in more than 500 cases as reported by Burns, and without any untoward results, is sufficient evidence as to its usefulness. One objection to its use is that the solution is prepared with some difficulty and is somewhat expensive if the prepared solution is purchased. To begin with, thorium nitrate is not a common salt and often can be obtained only on a special order, and even then from only a limited number of large chemical houses. After the salt is obtained, a considerable amount of concentrated sodium citrate solution is required to redissolve the thorium which at first is precipitated. The citrate solution so prepared must be made neutral by the addition of the proper amount of alkali. However, this solution, as has been shown, possesses certain disadvantages. Of greatest importance is the fact that it is much more viscid than the iodid solution, requiring over 50 per cent. more time for a given quantity to flow through the small tube of a viscometer. For this reason, under the same pressure much more of the iodid solution may be introduced into a kidney pelvis, for part of the capacity is always taken up by the urine excreted while the injection is taking place. Furthermore, the thorium solution has an osmotic pressure almost 50 per cent. greater than the iodid, and it is evident that the ideal solution should have an osmotic pressure still less than that of the iodid, at least not greater than that of a concentrated urine. The thorium solution is slightly, but definitely, more toxic than the iodid when given intravenously in dogs. In conclusion, it should be remembered that the molar iodid solution has an opacity distinctly greater than that of the standard thorium preparation and, in practice, seems to me to give greater contrast on plates, owing equally to its lower viscosity and greater opacity.

The 25 per cent. sodium bromid solution, which was recommended for pyelography by Weld some time after I had published two articles on the use of iodids for this purpose, naturally possesses many of the desirable features of the iodid solution. The chief advantages claimed for the bromid solution were that it was much less toxic than potassium iodid when given intravenously, and that it is much less expensive than any of the other mediums. It was also stated that in the same percentage concentrations the bromid and iodid solutions were of about equal opacity. These statements and their bearing on the selection of the most suitable medium for pyelography will be considered in greater detail. To begin with, the conclusion regarding the relative opacity of the bromid and iodid solutions is entirely erroneous. The fact that, when exposed to roentgen rays of the character of those used in pyelography, a molar (13.5 per cent.) solution of sodium iodid has the same, or greater, opacity than that possessed by a 3 molar (25.2 per cent.) solution of sodium bromid admits of no question. This has been established by my work as well as by previous investigations carried out by many physicists. And, in this connection, it is well to note again that there is no simple relation between the atomic weight of an element and its opacity to roentgen rays. It will also be noted that in his comparative toxicity tests, Weld used for the most part a 25 per cent. solution of sodium bromid against a 25 per cent. solution of potassium

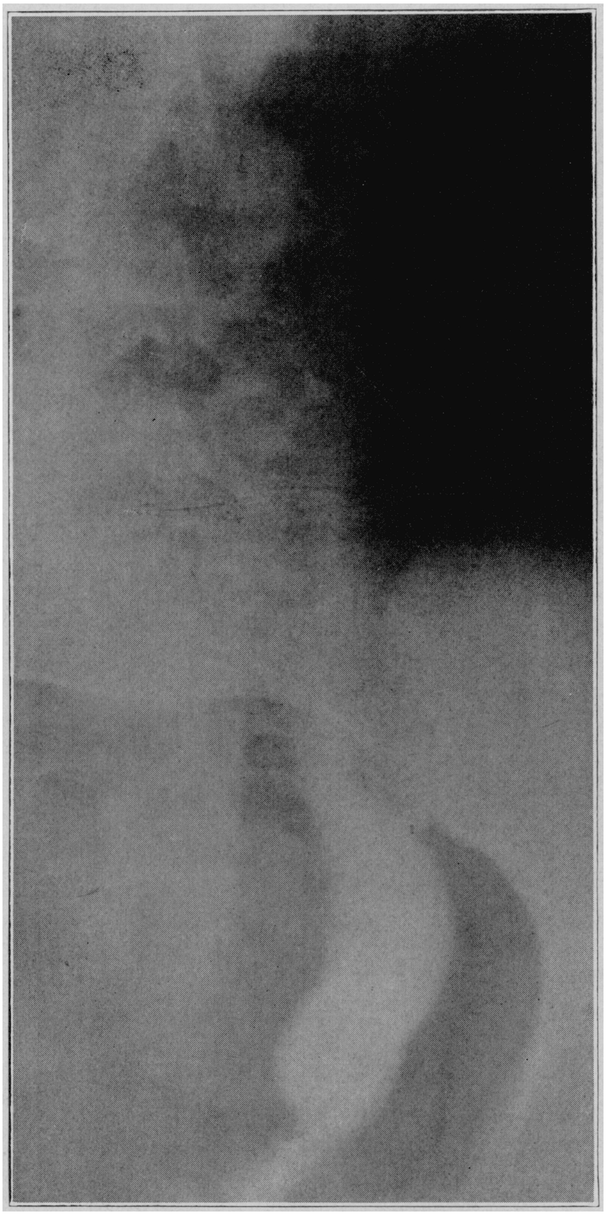

Fig. 9 (Mr. S.).—Left ureterogram with 13.5 per cent. sodium iodid solution. A shadow near the bladder seen in the original roentgenogram was localized by this ureterogram and can be seen in this plate as a dense center surrounded by a less dense zone lying at the lower end of the dilated ureter.

iodid. Even so, very little difference was found in the effect of these two solutions on the kidney parenchyma itself. But the great toxicity of potassium iodid when given intravenously in concentrated solution was especially emphasized. The marked toxicity of potassium salts when introduced into the blood stream, in pure and concentrated solutions, has been known for many years. If Weld had tested potassium bromid, he would have found it to be practically as toxic as the iodid, and, likewise, if he had tested sodium iodid, which I had even recommended as preferable to the potassium salt, he would have found it about as nontoxic as the sodium bromid, there being no appreciable difference in toxicity between a 25 per cent. solution of sodium iodid and sodium bromid when given intravenously in dogs. It is obvious, however, that for comparable results the molar (13.5 per cent.) sodium iodid and the 3 molar (25.2 per cent.) sodium bromid solutions must be used. When given intravenously, these solutions are relatively nontoxic, and when introduced into the kidney pelvis cause no apparent changes or diminution of function as shown by the usual tests. The question as to which of these two solutions is the better for pyelography probably will be established only after long experience. It is true that, as far as expense is concerned, the bromid solution would be preferable. A given volume of the bromid solution can be prepared at a cost much less than that of the same volume of iodid solution of the same opacity. However, at present, 200 c.c. of the iodid solution costs about $0.45; and, since on an average the amount of solution used for a pyelogram will not exceed 10 c.c., the cost is seen to be quite moderate and should not be a great factor in the selection of mediums unless they are to be used in very large quantities.

There are, however, several more or less valid reasons why, it appears to me, the iodid solution should be preferred:

1. It is very probable that the iodid solution is less irritating to a kidney pelvis than the bromid. At least, it may be stated definitely that the tongue is subjected to a more intense stimulation by the bromid solution.

2. It is very probable, though not definitely proved, that the molar iodid solution is less toxic to tissues in general, including kidney parenchyma, than the 25 per cent. bromid. The reasons for this statement are: first, a 25 per cent. solution of sodium iodid given intravenously in dogs has apparently no greater toxic effect than a 25 per cent. sodium bromid solution and the molar iodid solution, which is used in practice, is still less toxic; second, the 25 per cent. bromid solution has an osmotic pressure over three times as great as that of the iodid. This is a very important difference, as it is well known that, other conditions being equal, the toxicity of a solution to living tissues, in general, increases with the hypertonicity. It happens that the cells of the

kidney tubules and of the pelvis are undisturbed by the presence of the hypertonic urine; but the molar iodid solution has a still somewhat greater hypertonicity than urine and, in that respect, fails to meet the requirements of an ideal medium, and by so much the more does the bromid solution fail to meet this requirement.

3. The third quite real advantage possessed by the iodid solution is its marked relative increase in opacity to the roentgen ray as penetration increases. Physicists have commented on this property of iodin and have placed it in a group of elements exhibiting so-called selective absorption. This is of great practical importance in this way. Most of the technical difficulty in obtaining good pyelograms occurs in patients who have a great anteroposterior diameter at the level of the kidney, thus necessitating the use of greater roentgen-ray penetration. Under such conditions, the iodid solution casts a shadow which increases relatively in density as the penetration increases, while the bromid solution becomes relatively much less opaque. Therefore, to produce a shadow of the same relative density, a much stronger solution of the bromid must be used.

SUMMARY OF RESULTS

1. The investigation of the comparative opacity of several pyelographic mediums shows that the molar, or 13.5 per cent., solution of sodium iodid is fully as opaque as the 3 molar, or 25.2 per cent., solution of sodium bromid and is definitely more opaque than the standard neutral thorium solution, which is correctly designated as a 5/16 molar thorium nitrate solution, but is commonly called the "15 per cent." solution.

2. The kidney function as determined by the usual blood urea nitrogen and creatinin and by the phenolsulphonephthalein tests, both in the dog and in man, is not changed by the introduction of the molar and 4/3 molar solutions of sodium iodid into the kidney pelvis even when, experimentally, the latter was kept distended by the solutions at the secretory pressure of the kidney for twenty-five minutes. The same results were also obtained with the 3 molar sodium bromid solution.

3. When given intravenously in dogs, the 25 per cent. sodium iodid, as well as the 25 per cent. sodium bromid solution, produces no apparent immediate toxic effect. The blood pressure and respiration have remained unaffected when 50 c.c. of each of these solutions has been injected intravenously in a 30-pound dog within a period of ten minutes. The 13.5 per cent. sodium iodid solution, however, is the solution used for pyelography. Solutions of potassium salts, whether bromid or iodid, are very toxic when given intravenously, a fact long known

4. The comparatively rapid absorption of different substances from the kidney pelvis, as observed by Burns and Weld, is confirmed by the fact that the contents of the kidney pelvis of a dog one and a half to two hours after it has been filled with a molar or 4/3 molar sodium iodid solution, which was retained in the pelvis by occluding the ureter, fails to respond to the usual chemical tests for iodid.

5. The sensory stimulation or irritation of the kidney pelvis produced by the three different mediums investigated is probably very slight, but marked differences are obvious when tested on the tongue, the thorium solution causing the least stimulation and the 25 per cent. bromid, the greatest.

6. The viscosity of distilled water, the molar sodium iodid, the 3 molar sodium bromid and the standard thorium solutions, as determined by the ordinary viscometer, is represented by the figures 28, 29, 31.5 and 50, respectively. A low viscosity is a very important property for a good pyelographic medium, since the quantity of the medium which can be introduced into the kidney pelvis, other things being equal, varies inversely with the viscosity.

7. The osmotic pressure of an average concentrated urine, of the molar sodium iodid, the 3 molar sodium bromid and the standard thorium solution is represented by the figures 2.7, 3.78, 13.47 and 5.52, respectively. From this it is evident that the iodid solution is the least hypertonic of the three mediums, and in this respect is far nearer the ideal than the bromid solution which has over three times as great an osmotic pressure, for it is well known that, other things being constant, the injury produced by hypertonic solutions on living tissues increases with the hypertonicity.

8. For clinical use I have personally made twenty-two pyelograms, using sodium iodid varying in strength from 20 to 13.5 per cent. No serious reactions whatever have been seen. The number of patients who had more or less distress as a result of the pyelography is equaled by the number who suffered no additional discomfort whatever, and I am convinced that the additional discomfort was caused by overdistending the kidney pelvis.

9. In the light of the foregoing experiments my previous conclusions are modified in two respects: First, in the article that I published in collaboration with Grandy, sufficient emphasis was not placed on the fact that the sodium iodid solution was preferable to the potassium, for it has been shown that the potassium salt is somewhat irritating and, in addition, because of its toxicity when given intravenously, it does not afford so great a factor of safety in the event of its absorption in large amounts. Second, increasing experience has demonstrated that instead of the 25 per cent. solution of sodium iodid originally recommended, a molar or 13.5 per cent. solution has been found to be sufficiently

opaque for all pyelographic work, and in this respect, at least, it equals and, when penetrating rays are used, always surpassed the 25 per cent. bromid and the standard thorium solutions.

10. The molar, or 13.5 per cent., sodium iodid solution now recommended is prepared by dissolving 15 gm. of the salt in a sufficient amount of water to make 100 c.c. In previous articles I have shown that such a solution is neutral in reaction, mildly saline to taste, nonirritating, and does not form precipitates with blood or urine.

11. In conclusion, although the molar sodium iodid solution is not the least expensive of the pyelographic mediums, it nevertheless possesses certain distinct advantages which seem to me, at least, to make it the most suitable. Among these should be emphasized its freedom from toxic effects and irritation, as far as can be determined, its ease in preparation, the fact that it has the lowest viscosity and the lowest osmotic pressure of any mediums so far suggested, colloids and emulsions alone excepted, and the fact that it exhibits an opacity to roentgen rays which actually increases relatively with increasing penetration of the rays, definitely surpassing, in this respect, the thorium and bromid solutions.

Hope-Methodist Hospital.